Remarks:

Rejection under 35 U.S.C. § 102(b)

Claims 4-5 are rejected under 35 U.S.C. § 102(b). The Office Action states that these claims are "anticipated by Sheppard et al. (WO 98/42840A1) in view of the disclosure by Arena et al. (WO 97/21730A10)."

Applicant Response:

Applicants wish to call the Office's attention to the language of 35 U.S.C. § 102(b), which reads as follows:

> **"35 U.S.C. 102Conditions for patentability; novelty and loss of right to patent.**
> A person shall be entitled to a patent unless —
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States,"

There is provision in the language of the statute that allows for the Office to reject a claim under 35 U.S.C. § 102(b) based on one reference "in view of the disclosure" of a second reference.

Applicants have canceled these claims to expedite prosecution, but felt it necessary to clarify the specific requirement of the rejection.

Rejection under 35 U.S.C. § 102(e)

Claims 4-5 are rejected under 35 U.S.C. § 102(e). The Office states that these claims are "anticipated by US Patent No. 6,291,653B1, US patent No. 6,420,521B1, US patent No. 6,627,729B1, US patent No. 6,838,438B2, US patent No. 6,939,690B2 in light of the disclosure by Arena et al. (WO 97/21730A10)."

Applicant Response:

Again, Applicants wish to call the Office's attention to the language of 35 U.S.C. § 102(e), which reads as follows:

> **"35 U.S.C. 102 Conditions for patentability; novelty and loss of right to patent.**
> A person shall be entitled to a patent unless —
>
> (e) the invention was described in — (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States

> only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language; "

There is provision in the language of the statute that allows for the Office to reject a claim under 35 U.S.C. § 102(e) based on one reference "in view of the disclosure" of a second reference.

Applicants have canceled these claims to expedite prosecution, but felt it necessary to clarify the specific requirement of the rejection.

Rejection under 35 U.S.C. § 112

Claims 7, 9 and 10 are rejected under 35 U.S.C. § 112, first paragraph. The Office alleges that "the specification, while being enabling for discovering peptide of SEQ ID NO: 2 binding to the receptor encoding the amino acid of SEQ ID NO: 5, does not reasonably provide enablement for purifying the receptor encoding the amino acid residues comprising 41-326 of SEQ ID NO: 5 with the mobilized peptide or purification of said receptor expressing cell with said peptide." The Office Action states: "The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation." Applicants believe that the Office intended to state that this test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosure in the application coupled with information known in the art without undue experimentation, instead of "would undue experimentation".

The Office Action goes on to recite the factors outlined in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988), which include: "1). Nature of invention, 2). State of unpredictability of prior art, 3). Level of skill in the art, 4). Amount of direction presented by the specification; 5). Working examples taught by the specification; 6). Breath of claims, 7). Amount of the experimentation for making and using the invention commensurate in scope with these claims."

Applicants believe that there are several typographical errors in the Office Action. Respectfully, Applicants believe that the Office has attempted to address the Wands factors by stating that the "specification only teaches that applicants have identified the receptor of the peptide with the amino acid sequence of SEQ ID NO: 2 is one of know receptors of GHS-Rs with SEQ ID NO: 5. GHR-Rs are G-protein coupled receptors that are not exclusive for the claimed peptide binding. It is also no bound by other receptors in intro and in vivo."

Applicant believe that the Office intended to state: "GHS-Rs" instead of "GHR-Rs"; "known" instead of "know"; "not bound" instead of "no bound", and "in vitro" instead of "in intro".

The Office Action goes states that "the natural expression of said receptor is not very much clear and is very low in most cell types. Perhaps , it is predominantly expressed in pituitary cells." Additionally, the Office Action alleges that the specification does not teach whether the receptor /peptide binding is a reversible or non-reversible process, how the binding is disassociated with buffer, what kind of buffer is suitable. And the Office Action alleges it is well known in the art that the peptide binding to its receptor usually causes the receptor desensitization and internalization. Further, the Office Action states that the specification does not teach which cell population can be used for the purification, how a cell population can be purified. and that the specification does not have any working examples. for purifying either cell of peptide.

Applicant Response:

Applicants respectfully traverse this rejection.

Applicants do not believe that the Office has established a case of non-enablement in the present Office Action. Section 2164.01(a) of the Manual of Patent Examining Procedure describes the "Undue Experimentation Factors" and states:

> "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:
>
> (A) The breadth of the claims;
> (B) The nature of the invention;
> (C) The state of the prior art;
> (D) The level of one of ordinary skill;
> (E) The level of predictability in the art;
> (F) The amount of direction provided by the inventor;
> (G) The existence of working examples; and
> (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure."

Furthermore, Section 2164.01(a) of the Manual of Patent Examining Procedure states:

> "It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement

must be based on the evidence as a whole. 858 F.2d at 737, 740, 8 USPQ2d at 1404, 1407.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404."

Applicants do not believe that the Office has met its burden set forth in Section 2164.01(a) of the Manual of Patent Examining Procedure, requiring the Office to consider **all** the evidence related to **each** of the Wands factors, requiring that any conclusion of nonenablement be based on the evidence as a whole nor by weighing all of the factual considerations.

The instant specification teaches the discovery of the formation of a peptide-receptor complex between the polypeptide of SEQ ID NO: 2 and the GHS-R of SEQ ID NO: 5, and that this peptide-receptor formation can be used to purify the polypeptide of SEQ ID NO: 2 by immobilizing cells-expressing the receptor or to purify the receptor of SEQ ID NO: 5 by immobilizing the polypeptide of SEQ ID NO: 2. The specification teaches that the peptide binds to a GHS-R and that such binding is expected in tissues such as stomach, small intestine, pancreas, lung, kidney, duodenum, jejunum, and brain. See for example, page 10, lines 1-4 and Example 9, pages 82-84. See also, page 65, lines18-28.

Furthermore the instant specification teaches on page 64, lines 4-15:

"GHS-R can also be used for purification of zsig33. The polypeptide (i.e., SEQ ID NO:5) is immobilized on a solid support, such as beads of agarose, cross-linked agarose, glass, cellulosic resins, silica-based resins, polystyrene, cross-linked polyacrylamide, or like materials that are stable under the conditions of use. Methods for linking polypeptides to solid supports are known in the art, and include amine

chemistry, cyanogen bromide activation, N-hydroxysuccinimide activation, epoxide activation, sulfhydryl activation, and hydrazide activation. The resulting medium will generally be configured in the form of a column, and fluids containing zsig33 polypeptides are passed through the column one or more times to allow zsig33 polypeptides to bind to GHS-R polypeptides. The zsig33 polypeptide is then eluted using changes in salt concentration, chaotropic agents (guanidine HCl), or pH to disrupt receptor binding."

Thus, the specification teaches methods for purifying the polypeptide of SEQ ID NO: 2.

Nonetheless, to expedite prosecution, Claims 7 and 9 have been amended to recite methods of identifying cells expressing the GHS-R of SEQ ID NO: 5 and Claim 10 has been amended to methods of identifying agonists to the polypeptide of SEQ ID NO: 2. These amendments overcome any lack of enablement based on an analysis of the Wands factors. Support for these claim amendments can be found throughout the specification. See, for example, page 47, line 26 to page 48, line 9:

"Cells expressing functional GHS-R are used within screening assays. A variety of suitable assays are known in the art. These assays are based on the detection of a biological response in the target cell. One such assay is a cell proliferation assay. Cells are cultured in the presence or absence of a test compound, and cell proliferation is detected by, for example, measuring incorporation of tritiated thymidine or by colorimetric assay based on the metabolic breakdown of Alymar BlueTM (AccuMed, Chicago, IL) or 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) (Mosman, J. Immunol. Meth. 65: 55-63, 1983). Alternative assays are also listed herein.

Another assay uses phospholipase C signal transduction to measure receptor binding. An exemplary assay of this sort measures release of Ca2+ with aequorin, a bioluminescent Ca2+-sensitive reporter protein. This assay is further described by Feighner, S.D. et al., supra. Hence, zsig33 peptides can be tested using an assay that measures phospholipase C transduction."

See also page 50, lines 23-31; page 59, lines 4-13;

New Claim 27

Claim 27 has been newly added to claim that the peptide-receptor complex formation described in the specification can be used to identify antagonists of the peptide as well. See previous paragraph for support for this new claim. See also, page 62, line 8, to page 63, line 23.

Reconsideration of the application in view of the above amendments and following remarks is requested. Claims 7, 9, 10 and 27 are now in the case. Claim(s) 7, 9, and 10 have been amended. Claim(s) 4, and 5 have been canceled. Claim 27 is newly added. Applicant(s) assert(s) that the present amendment adds no new matter.

Applicants reserve the right to prosecute claims to cancelled subject matter in one or more continuing applications.

On the basis of the above amendments and remarks, Applicants believe that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6752.

The total fees, estimated to be $1050.00, will be paid via the USPTO EFS.

Respectfully Submitted,

Robyn Adams
Registration No. 44,495

Enclosures:
Petition and Fee for Extension of Time

Customer No. 10117
ZymoGenetics, Inc